Claims

1. A method for identifying antifungal agents comprising

i. incubating, with at least one candidate compound, a fungal GTP cyclohydrolase II polypeptide under conditions allowing the binding of the candidate compound to the fungal GTP cyclohydrolase II; and

ii. selecting, by step ii), at least a candidate compound which binds to the fungal GTP cyclohydrolase II of step i); or

iii. selecting, by step iii), at least one candidate compound which reduces or blocks the activity of the fungal GTP cyclohydrolase II of step i); or

iv. selecting, by step iv), at least one candidate compound which inhibits or decreases transcription, translation or expression of the fungal GTP cyclohydrolase II of step i).

2. A method as claimed in claim 1, wherein the fungal GTP cyclohydrolase II is encoded by a nucleic acid sequence comprising

a) a nucleic acid sequence shown in SEQ ID NO:1; or

b) a nucleic acid sequence which, owing to the degeneracy of the genetic code, can be deduced from the amino acid sequence shown in SEQ ID NO: 2 by back translation; or

c) a nucleic acid sequence which, owing to the degeneracy of the genetic code, can be deduced from a functional equivalent of the amino acid sequence shown in SEQ ID NO: 2, which has an identity with SEQ ID NO:2 of at least 49%, by back translation.

3. A nucleic acid sequence comprising

a) a nucleic acid sequence shown in SEQ ID NO:4; or

b) a nucleic acid sequence which, owing to the degeneracy of the genetic code, can be deduced from the amino acid sequence shown in SEQ ID NO:5 by back translation; or

c) a nucleic acid sequence which, owing to the degeneracy of the genetic code, can be deduced from a functional equivalent of the amino acid sequence shown in SEQ ID NO:5, which has an identity with SEQ ID NO:5 of at least 66%, by back translation.

4. A method as claimed in claim 1 or 2 which comprises testing a candidate compound in a fungal GTP cyclohydrolase II inhibition assay.

5. A method as claimed in claim 4 which comprises

a) incubating, with a candidate compound, a fungal GTP cyclohydrolase II in a cell free system;

b) selecting, by step b), a candidate compound which decreases the activity of the fungal GTP cyclohydrolase II.

6. A method as claimed in claim 5, wherein the enzymatic activity of the fungal GTP cyclohydrolase II is determined in comparison to the activity of a fungal GTP cyclohydrolase II not incubated with the candidate compound.

7. A method for determination of GTP cyclohydrolase I or II activity comprising the steps of

a) adding GTP or GTP analog, NAD+ and formate dehydrogenase to a sample comprising GTP cyclohydrolase II or I; and

b) determination of the NAPH content.

8. A method as claimed in claim 5 or 6, wherein the enzymatic activity of GTP cyclohydrolase II is determined according to claim 7.

9. A method for identification of inhibitors of GTP cyclohydrolase I or II comprising the following steps:

a) adding GTP or GTP analog, NAD+ and formate dehydrogenase to a sample comprising GTP cyclohydrolase I or II;

b) adding formate, NAD+ and formate dehydrogenase to a second sample comprising GTP cyclohydrolase I or II;

c) adding to the sample of step a) and step b) a candidate compound;

d) determining the activity of both samples;

e) selecting candidate compounds that show inhibition in the presence of GTP and no inhibition in the presence of formic acid.

10. A method as claimed in claim 5 or 6, wherein inhibitors of fungal fungal GTP cyclohydrolase II are identified in an inhibition assay according to claim 9.

11. A method as claimed in any of claims 5, 6, 8 and 10, wherein GTP is used as substrate and the NADPH content is determined by monitoring the increase in the absorption at 340nm.

12. A method as claimed in claim 1, 2 or 4 comprising the following steps:

a) the generation of organisms which, following transformation with a nucleic acid sequence encoding GTP cyclohydrolase II are capable of overexpressing polypeptide with GTP cyclohydrolase II activity;

b) the application, to the organism of step a) and to an analogous, untransformed organism, of a candidate compound;

c) the determination of the growth, the viability or infectivity of the transgenic and the untransformed organism following application of the substance of step b);

d) the selection of candidate compounds, which reduces growth, viability or infectivity of the transgenic and the untransformed fungi following application of the substance of step b).

13. A method as claimed in claim 12, wherein the organism is a fungus.

14. A method as claimed in any of claims 1, 2, 4 to 6, 8 and 10 to 13, wherein the substances are identified in a high-throughput screening.

15. A method as claimed in any of claims 1, 2, 4 to 6, 8, 10 to 14, wherein the antifungal agent identified via the method is applied to a phytopathogenic fungus in order to verify the fungicidal activity.

16. An antifungal agent identified via one of the methods as claimed in any of claims 1, 2, 4 to 6, 8, and 10 to 15.

17. A process for the preparation of a fungicidal composition, which comprises

a) identifying a antifungal agent via one of the methods as claimed in any of claims 1, 2, 4 to 6, 8 and 10 to 15, and

b) formulating the antifungal agent identified via (a), or an agriculturally useful salt of the active ingredient identified via (a), with suitable adjuvants.

18. The use of compounds as claimed in claim 16 for producing drugs.

19. A process for the preparation of a pharmaceutical fungicidal composition, which comprises

a) identifying an antifungal agent via one of the methods as claimed in any of claims 1, 2, 4 to 6, 8 and 10 to 15, and

b) formulating the antifungal agent identified via (a), or a pharmaceutically useful salt of the active ingredient identified via (a), with suitable excipients.

20. A method for controlling harmful fungi, which comprises treating the fungi, or the materials, plants, soils or seeds to be protected from fungal infection, with an effective amount of a fungicidal compound as claimed in claim 16 or a fungicidal composition prepared according to claim 19.

21. The use of a fungal GTP cyclohydrolase as target for the identification of antifungal agents.